KM

Day : Tuesday
Date: 9/21/2004

Time: 09:26:18

PALM INTRANET

Inventor Information for 10/743740

Inventor Name	City	State/Country
IISHI, EIICHI	OSAKA	JAPAN
IMAMIYA, YOSHIYUKI	OSAKA	JAPAN

Appln Info | Contents | Petition Info | Atty/Agent Info | Continuity Data | Foreign Data

Search Another: Application# [ ] Search **or Patent#** [ ] Search

PCT / [ ] / [ ] Search **or PG PUBS #** [ ] Search

Attorney Docket # [ ] Search

Bar Code # [ ] Search

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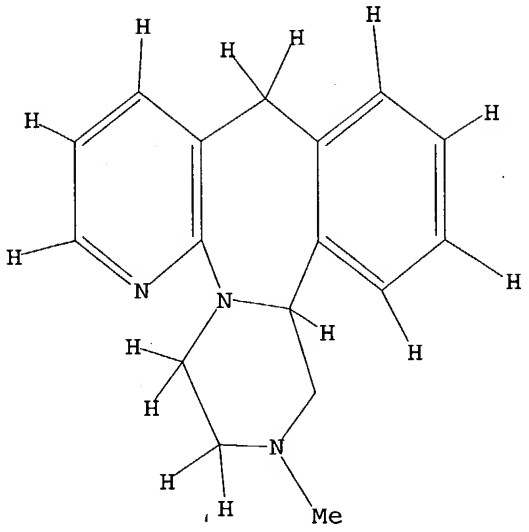
L Number	Hits	Search Text	DB	Time stamp
1	163	540/578.ccls.	USPAT	2004/09/21 09:25
2	84	540/578.ccls. and anhydrous$	USPAT	2004/09/21 09:25

L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -     232 TO ITERATE

100.0% PROCESSED     232 ITERATIONS                                 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          3727 TO     5553
PROJECTED ANSWERS:                2 TO      124

L2             2 SEA SSS SAM L1

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100.0% PROCESSED    4747 ITERATIONS                                29 ANSWERS
SEARCH TIME: 00.00.01

L3            29 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   155.42     155.63

FILE 'CAPLUS' ENTERED AT 09:42:56 ON 21 SEP 2004
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FILE COVERS 1907 - 21 Sep 2004 VOL 141 ISS 13
FILE LAST UPDATED: 20 Sep 2004 (20040920/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 391 L3

=> s l4 and (anhydrou? or crystal?)
L5 12 L4 AND (ANHYDROU? OR CRYSTAL?)

=> d ibib abs hitstr tot

L5 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:570816 CAPLUS
DOCUMENT NUMBER: 139:138735
TITLE: Sedative non-benzodiazepine formulations
INVENTOR(S): O'Toole, Edel; Fogarty, Siobhan
PATENT ASSIGNEE(S): Biovail Laboratories Inc., Barbados
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059349	A1	20030724	WO 2003-IE1	20030109

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

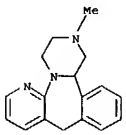
PRIORITY APPLN. INFO.: US 2002-346613P P 20020110

AB The invention provides for an enhanced absorption pharmaceutical composition comprising a plurality of microparticles, each microparticle comprising at least one sedative non-benzodiazepine, at least one spheronisation aid, and at least one solubility enhancer. The microparticles of the invention are further incorporated into an oral fast-dispersing dosage form. For example, microparticles were prepared containing zolpidem tartrate 15%, Gelucire 50/13 35%, and distilled monoglyceride (Myvaplex) 50%. Microparticles obtained were then coated for taste masking with a coating solution containing a 60:30:10 ratio of Eudragit NE30D, talc, and Methocel. The coated microparticles were used for preparation of tablets.

IT **85650-52-8**, Mirtazapine
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of microparticles for enhanced oral bioavailability of non-benzodiazepine sedatives)

RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)

L5 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

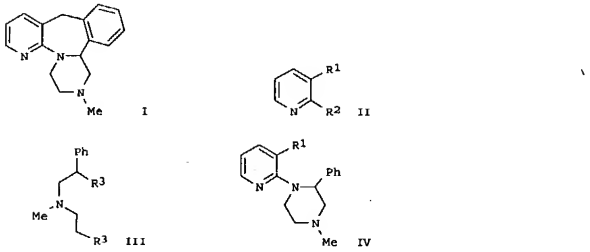
L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:282146 CAPLUS
DOCUMENT NUMBER: 138:304301
TITLE: Novel synthesis and **crystallization** of piperazine ring-containing compounds such as mirtazapine
INVENTOR(S): Singer, Claude; Liberman, Anita; Finkelstein, Nina
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U.S. Ser. No. 552,485.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003069417	A1	20030410	US 2002-206344	20020729
US 2001051718	A1	20011213	US 2001-900646	20010706
US 6545149	B2	20030408		
US 2003088094	A1	20030508	US 2002-283093	20021030
US 6576764	B2	20030610		
US 2003120068	A1	20030626	US 2003-348757	20030123
US 2003135043	A1	20030717	US 2003-368441	20030220
US 2004176591	A1	20040909	US 2004-800918	20040316

PRIORITY APPLN. INFO.: US 1999-130047P P 19990419
US 2000-182745P P 20000216
US 2000-552485 A2 20000418
US 2001-900646 A3 20010706
US 2002-283093 A3 20021030
US 2003-368441 B1 20030220

OTHER SOURCE(S): CASREACT 138:304301; MARPAT 138:304301
GI

L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

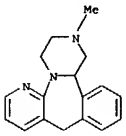


AB Mirtazapine (I) was prepared by reacting substituted pyridine II [R1 = CH2OH, CH2Cl, CH2Br, CH2I; R2 = NH2] with compound III [R3 = Cl, F, Br, I] followed by treating the resulting piperazine IV with ring closing reagent, such as H2SO4. The mirtazapine intermediate IV (R1 = CO2H) may be prepared by hydrolyzing IV (R1 = CN) with KOH at a temperature of at least about 140°C. New processes for recrystn. of I form crude mirtazapine are also disclosed. The present invention also relates to **crystalline** adducts of mirtazapine and water, preferably containing up to about 3.5% by weight water, pharmaceutical compns. containing the **cryst**. adducts, and methods of treating depression by administering such compns.

IT **341512-90-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and **crystallization** of mirtazapine water adduct)

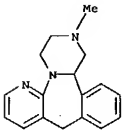
RN 341512-90-1 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl-, hydrate (9CI) (CA INDEX NAME)

L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

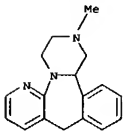


●x H_2O

IT **85650-52-8P**, Mirtazapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and **crystallization** of piperazine ring-containing compds. such as mirtazapine)
RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:695977 CAPLUS
DOCUMENT NUMBER: 137:216962
TITLE: Methods for the preparation of mirtazapine intermediates
INVENTOR(S): Metzger, Leonid; Wizel, Shlomit
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

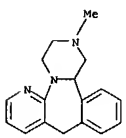
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070513	A1	20020912	WO 2002-US4340	20020214
WO 2002070513	C2	20021121		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002165238	A1	20021107	US 2002-73960	20020214
US 6774230	B2	20040810		
EP 1370549	A1	20031217	EP 2002-714893	20020214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2001-272699P	P 20010301
			WO 2002-US4340	W 20020214

OTHER SOURCE(S): CASREACT 137:216962
AB The preparation of 1-(3-carboxy-2-pyridyl)-4-methyl-2-phenylpiperazine dihydrate (I) and other mirtazapine intermediates are described. These compds. are particularly useful in the preparation of mirtazapine. Thus, 1-(3-cyano-2-pyridyl)-4-methyl-2-phenylpiperazine was hydrolyzed with aqueous KOH, neutralized with HCl and the precipitate washed with water to give I whose **crystal** structure is reported.
IT **85650-52-8P**, Mirtazapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of 1-(3-carboxy-2-pyridyl)-4-methyl-2-phenylpiperazine dihydrate as an intermediate for mirtazapine)
RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:406942 CAPLUS
DOCUMENT NUMBER: 136:401782
TITLE: Process for the manufacture of **anhydrous**, solvent-free mirtazapine **crystals**
INVENTOR(S): Maeda, Chiharu; Yoshikawa, Sadanobu; Iishi, Eiichi
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1209159	A2	20020529	EP 2001-111102	20010508
EP 1209159	A3	20030305		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002065413	A1	20020530	US 2001-842871	20010427
US 6660730	B2	20031209		
AU 2001040301	A5	20020606	AU 2001-40301	20010430
JP 2002220390	A2	20020809	JP 2001-291863	20010925
PRIORITY APPLN. INFO.:			JP 2000-359891	A 20001127

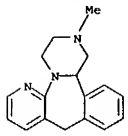
OTHER SOURCE(S): CASREACT 136:401782
AB Methods for producing **anhydrous** mirtazapine **crystals** that are either (1) substantially free of lower alc. insolubles or (2) substantially free of residual solvent, and which have an average particle diameter of from 10-50 μm, are described where: one filters a lower alc. (e.g., methanol) solution of crude mirtazapine to provide a filtrate; concentrating the filtrate to provide a concentrated filtrate; and **crystallising** the **anhydrous** mirtazapine from the concentrated filtrate using a precipitation solvent selected from heptane and petroleum ethers.
IT **85650-52-8P**, Mirtazapine
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); PYP (Physical process); PREP (Preparation); PROC (Process)
(process for the manufacture of **anhydrous** solvent-free mirtazapine **crystals**)
RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L5 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:880108 CAPLUS
DOCUMENT NUMBER: 136:268247
TITLE: Spectroscopic methods for determining enantiomeric purity and absolute configuration in chiral pharmaceutical molecules
AUTHOR(S): Shah, Rekha D.; Nafie, Laurence A.
CORPORATE SOURCE: The RW Johnson Pharmaceutical Research Institute, Spring House, PA, 19477-0776, USA
SOURCE: Current Opinion in Drug Discovery & Development (2001), 4(6), 764-775
CODEN: CODDFF; ISSN: 1367-6733
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with refs. Anal. support, such as methods development, along with identification and characterization of intermediates and impurities, are critical in the development of a chemical process. The preparation of a drug substance requires the development of anal. methods for monitoring reactions and identifying impurities. Methods development for a chiral drug mol. is more difficult as the method must be capable of monitoring the overall reaction as well as possible racemization of starting materials and products. Chiral methods are often required to monitor the reaction steps of a synthesis, however, the development of enantiomeric purity methods are time-consuming and expensive. The use of chiroptical detectors, such as CD (CD), optical rotation (OR) and vibrational CD (VCD), can help to reduce or eliminate the need to develop chiral monitoring methods and also to predict absolute configuration. Recently, VCD has shown remarkable success with the latter and currently holds the most promise as a general, direct method that can be used as an alternative to X-ray **crystallog.** Each of the mentioned techniques can help anal. chemists to reduce the time associated with traditional enantiomeric purity methods development and to determine absolute configuration. This review will discuss the scope and limitations of these techniques for the rapid and routine determination of both enantiomeric excess and absolute configuration.
IT **85650-52-8**, Mirtazapine
RL: ANT (Analyte); ANST (Analytical study)
(spectroscopic methods for determining enantiomeric purity and absolute configuration in chiral pharmaceuticals)
RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)

L5 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:435071 CAPLUS
DOCUMENT NUMBER: 135:33494
TITLE: Process for the preparation of a pyridinemethanol compound
INVENTOR(S): Iishi, Eiichi; Yoshikawa, Kanami
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042240	A1	20010614	WO 2000-JP6688	20000928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2001042239	A1	20010614	WO 2000-JP5384	20000811
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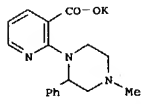
AU 2000074472	A5	20010618	AU 2000-74472	20000928
AU 771484	B2	20040325		
EP 1238977	A1	20020911	EP 2000-962909	20000928
EP 1238977	B1	20031126		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AT 255103	E	20031215	AT 2000-962909	20000928
PRIORITY APPLN. INFO.:			JP 1999-353514 A	19991213
			WO 2000-JP5384 W	20000811
			WO 2000-JP6688 W	20000928

OTHER SOURCE(S): CASREACT 135:33494
GI

L5 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

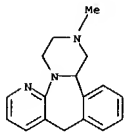


AB A pyridinemethanol compound useful as an important intermediate for the preparation of mirtazapine effective as an antidepressant can be prepared by reducing a potassium salt of pyridinecarboxylic acid as represented by formula I with a metal hydride. Thus, 1-butanol 162, KOH 60.93, and 2-(4-methyl-2-phenylpiperazin-1-yl)pyridine-3-carbonitrile oxalate 40 g were heated to give potassium 2-(4-methyl-2-phenylpiperazin-1-yl)pyridine-3-carboxylate, which was reduced in THF with 12.5 g lithium aluminum hydride to give 21.78 g 2-(4-methyl-2-phenylpiperazin-1-yl)pyridine-3-methanol (yield 70.78%).

IT **85650-52-8P**, Mirtazapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyridinemethanol compound as intermediate for mirtazapine)

RN 85650-52-8 CAPLUS

CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:435070 CAPLUS
DOCUMENT NUMBER: 135:33493
TITLE: Process for the preparation of a pyridinemethanol compound
INVENTOR(S): Iishi, Eiichi; Yoshikawa, Kanami
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042239	A1	20010614	WO 2000-JP5384	20000811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000064742	A5	20010618	AU 2000-64742	20000811
WO 2001042240	A1	20010614	WO 2000-JP6688	20000928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000074472	A5	20010618	AU 2000-74472	20000928
AU 771484	B2	20040325		
EP 1238977	A1	20020911	EP 2000-962909	20000928
EP 1238977	B1	20031126		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AT 255103	E	20031215	AT 2000-962909	20000928
PT 1238977	T	20040331	PT 2000-962909	20000928
ES 2209985	T3	20040701	ES 2000-962909	20000928
US 6376668	B1	20020423	US 2000-706803	20001107
US 2002035255	A1	20020321	US 2001-981919	20011019
US 6437120	B2	20020820		

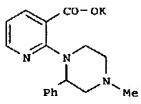
PRIORITY APPLN. INFO.:

JP 1999-353514	A	19991213
WO 2000-JP5384	W	20000811
WO 2000-JP6688	W	20000928
US 2000-706803	A3	20001107

L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

OTHER SOURCE(S): CASREACT 135:33493

GI

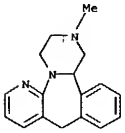


AB A pyridinemethanol compound serving as an important intermediate of mirtazapine useful as antidepressant can be prepared by reducing a potassium salt of a pyridinecarboxylic acid as represented by formula I with a metal hydride.

IT **85650-52-8P**, Mirtazapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyridinemethanol compound as intermediate for mirtazapine)

RN 85650-52-8 CAPLUS

CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:396869 CAPLUS
DOCUMENT NUMBER: 135:12413
TITLE: **Anhydrous** mirtazapine **crystals** and process for the production thereof
INVENTOR(S): Iishi, Eiichi; Mamiya, Yoshiyuki
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038330	A1	20010531	WO 2000-JP6687	20000928
W: AU, CA, IN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO 2001038329	A1	20010531	WO 2000-JP4835	20000719
W: AU, CA, IN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1225174	A1	20020724	EP 2000-962908	20000928
EP 1225174	B1	20040317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 261966	E	20040415	AT 2000-962908	20000928

PRIORITY APPLN. INFO.:

JP 1999-333049	A	19991124
JP 2000-67476	A	20000310
WO 2000-JP4835	W	20000719
WO 2000-JP6687	W	20000928

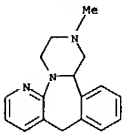
AB This document discloses : lowly hygroscopic **anhydrous** mirtazapine **crystals** exhibiting a moisture absorption of as low as 0.6 weight% (or below) when stored for 500 h in the air under the conditions of 25°C, relative humidity of 75% and atmospheric pressure; a process for the production of **anhydrous** mirtazapine **crystals** ; **crystals** of mirtazapine hydrates and a process for the production thereof. According to the process, stable **anhydrous** mirtazapine **crystals** exhibiting low hygroscopicity can be produced by a simple industrial method, and the obtained **anhydrous** mirtazapine **crystals** are suitably usable as an antidepressant by virtue of their extremely low hygroscopicity.

IT **341512-89-8P 341512-90-1P**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(**anhydrous** mirtazapine **crystals** and process for production thereof)

RN 341512-89-8 CAPLUS

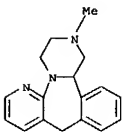
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl-, hydrate (2:1) (9CI) (CA INDEX NAME)

L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



●1/2 H_2O

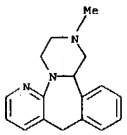
RN 341512-90-1 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl-, hydrate (9CI) (CA INDEX NAME)



●x H_2O

IT **85650-52-8P**, Mirtazapine
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**anhydrous** mirtazapine **crystals** and process for production thereof)
RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)

L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

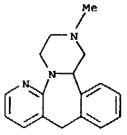
L5 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:396868 CAPLUS
DOCUMENT NUMBER: 135:12412
TITLE: **Anhydrous** mirtazapine **crystals** and process for producing the same
INVENTOR(S): Iishi, Eiichi; Imamiya, Yoshiyuki
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038329	A1	20010531	WO 2000-JP4835	20000719
W: AU, CA, IN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 2000060199	A5	20010604	AU 2000-60199	20000719
WO 2001038330	A1	20010531	WO 2000-JP6687	20000928
W: AU, CA, IN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 2000074471	A5	20010604	AU 2000-74471	20000928
AU 763502	B2	20030724		
EP 1225174	A1	20020724	EP 2000-962908	20000928
EP 1225174	B1	20040317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 261966	E	20040415	AT 2000-962908	20000928
US 2002103372	A1	20020801	US 2002-41495	20020110
US 6552189	B2	20030422		
US 2003130504	A1	20030710	US 2003-337277	20030107
US 6723845	B2	20040420		
US 2004138447	A1	20040715	US 2003-743740	20031224

PRIORITY APPLN. INFO.:
JP 1999-333049 A 19991124
JP 2000-67476 A 20000310
WO 2000-JP4835 W 20000719
WO 2000-JP6687 W 20000928
US 2000-697329 A3 20001027
US 2002-41495 A3 20020110
US 2003-337277 A3 20030107

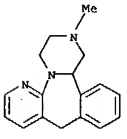
AB This document discloses : lowly-hygroscopic **anhydrous** mirtazapine **crystals** showing moisture absorption of 0.6 weight% or less when stored in the air at 25°C, at a relative humidity of 75% under atmospheric
pressure for 500 h; a process for producing **anhydrous** mirtazapine **crystals** showing moisture absorption of 0.6 weight% or less when stored in the air at 25°C at a relative humidity of 75% under atmospheric pressure for 500 h characterized by drying **crystals** of mirtazapine hydrate; and a process for producing **crystals** of

L5 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
mirtazapine hydrate characterized by **crystg.** crude mirtazapine by using a water sol. polar org. solvent and water. By using this prodn. method, stable **anhyd.** mirtazapine having little hygroscopicity can be produced by a convenient industrial method. The **anhyd.** mirtazapine **crystals** are usable as active ingredients in an antidepressant.
IT **341512-89-8 341512-90-1**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(preparation of **anhydrous** mirtazapine **crystals**)
RN 341512-89-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl-, hydrate (2:1) (9CI) (CA INDEX NAME)



●1/2 H_2O

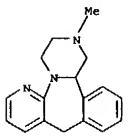
RN 341512-90-1 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl-, hydrate (9CI) (CA INDEX NAME)



●x H_2O

IT **85650-52-8P**, Mirtazapine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **anhydrous** mirtazapine **crystals**)
RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)

L5 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

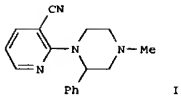
L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:265372 CAPLUS
DOCUMENT NUMBER: 134:280862
TITLE: Process for the preparation of a piperazine derivative
INVENTOR(S): Maeda, Chiharu; Iishi, Eiichi; Wang, Weigi; Imamiya, Yoshiyuki
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025185	A1	20010412	WO 2000-JP5432	20000814
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2001023345	A1	20010405	WO 2000-JP6650	20000927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1136470	A1	20010926	EP 2000-962874	20000927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 751629	B2	20020822	AU 2000-74455	20000927
US 6495685	B1	20021217	US 2000-697140	20001027
PRIORITY APPLN. INFO.:			JP 1999-280378 A	19990930
			WO 2000-JP5432 W	20000814
			WO 2000-JP6650 W	20000927

OTHER SOURCE(S): CASREACT 134:280862
GI

L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



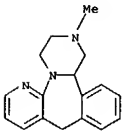
I

AB A process for the preparation of a piperazine derivative, namely 2-(4-methyl-3-phenylpiperazin-1-yl)-3-cyanopyridine (I), comprises reacting 1-methyl-3-phenylpiperazine with 2-chloro-3-cyanopyridine in the presence of a base and an alkali metal halide in an aprotic polar organic solvent. This piperazine derivative I and its oxalate are useful as intermediates for the preparation of mirtazapine. Thus, 11.4 kg N-methylethanolamine was added dropwise to a solution of 20 kg styrene oxide in 38 kg DMF at .apprx.80°, stirred at .apprx.80° for 3 h, and cooled to room temperature to give a DMF solution of N-(2-hydroxyethyl)-N-methyl-2-hydroxy-2-phenylethylamine which was added dropwise to a solution of 45 kg SOCl2 in 67.4 kg toluene at 0-25°, stirred at 45-55° for 2 h, cooled at ≤25°, treated dropwise with 95 kg H2O and then with 30 weight% aqueous KOH at 0-25°, and left to stand for phase separation. The organic and aqueous phase were separated and the aqueous phase was extracted with 55 kg toluene, followed by combining the extract and the organic phase, drying over 4.8 kg MgSO4, treating with 4.8 kg activated clay and filtration, and washing with 19.9 kg PhMe to give a toluene solution of N-(2-chloroethyl)-N-methyl-2-chloro-2-phenylethylamine (II). To the toluene solution was introduced 5.5 kg HCl(g) at 10-35° and stirred at 20-25° for 2 h and the precipitated **crystals** were filtered and washed with 69 kg toluene to give 30 kg II.HCl. EtOAc (100 mL), 460 mg Bu4NBr, and 20.1 g II.HCl were added to 132 g 28% aqueous NH3 at room temperature and stirred at 40-45° for 3 h, followed by separating the organic layer and extracting the aqueous layer with EtOAc (2 + 30 mL) and the combined organic layer evaporated in vacuo to give 53.8% 1-methyl-3-phenylpiperazine (III) (7.1 g). III 5.51, 2-chloro-3-cyanopyridine 4.47, Et3N 4.1, and KI 5.20 g were added to 11 mL DMF and stirred at 125-130° for 24 h, followed by removing Et3N and DMF under reduced pressure, adding 20 mL H2O and 25 mL EtOAc to the residue, adjusting pH at 8-9 with 10% NaOH, separating the organic phase, and extracting the aqueous layer with EtOAc (3 + 30 mL), washing the combined the organic layer with 5% NaHCO3, drying and concentration, and crystallization from petroleum ether 36% I (3.14 g, 97.1% purity).

IT **85650-52-8P**, Mirtazapine
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of (methylphenylpiperazinyl)cyanopyridine as

L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
mirtazapine)

RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

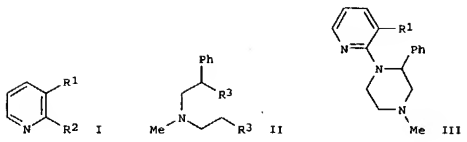
FORMAT

L5 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:756528 CAPLUS
DOCUMENT NUMBER: 133:321900
TITLE: Novel synthesis and **crystallization** of piperazine ring-containing compounds such as mirtazapine
INVENTOR(S): Singer, Claude; Liberman, Anita; Pinkelstein, Nina
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

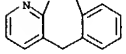
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000062782	A1	20001026	WO 2000-US10357	20000418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000043577	A5	20001102	AU 2000-43577	20000418
TR 200103028	T2	20020121	TR 2001-200103028	20000418
EP 1178805	A1	20020213	EP 2000-923457	20000418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2004500324	T2	20040108	JP 2000-611918	20000418
ZA 2001008220	A	20021205	ZA 2001-8220	20011005
HR 2001000747	A1	20021231	HR 2001-747	20011015
US 2003088094	A1	20030508	US 2002-283093	20021030
US 6576764	B2	20030610		
US 2003120068	A1	20030626	US 2003-348757	20030123
US 2004176591	A1	20040909	US 2004-800918	20040316
PRIORITY APPLN. INFO.:			US 1999-130047P	P 19990419
			US 2000-182745P	P 20000216
			US 2000-552485	A3 20000418
			WO 2000-US10357	W 20000418
			US 2001-900646	A3 20010706
			US 2002-283093	A3 20021030
			US 2003-368441	B1 20030220

OTHER SOURCE(S): CASREACT 133:321900; MARPAT 133:321900
GI

L5 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



AB Mirtazapine, useful in treating depression (no data), was prepared by reacting pyridine I [R1 = CH2OH, CH2Cl, CH2Br, CH2I; R2 = NH2] with compound II [R3 = Cl, F, Br, I] followed by treating the resulting piperazine III with H2SO4. The mirtazapine intermediate 1-(3-carboxypyridyl-2)-4-methyl-2-phenylpiperazine may be made by hydrolyzing 1-(3-cyanopyridyl-2)-4-methyl-2-phenylpiperazine with KOH at a temperature of at least about 130°C. The present invention also relates to new processes for recrystn. of mirtazapine form crude mirtazapine.
IT **85650-52-8P**, Mirtazapine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel synthesis and **crystallization** of piperazine ring-containing compds. such as mirtazapine)
RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



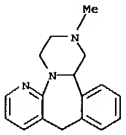
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:753085 CAPLUS
DOCUMENT NUMBER: 132:458
TITLE: Use of tricyclic antidepressants for local analgesia
INVENTOR(S): Sawynok, Jana; Esser, Mike; Reid, Allison
PATENT ASSIGNEE(S): Dalhousie Univeraity, Can.
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959598	A1	19991125	WO 1999-CA449	19990519
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6211171	B1	20010403	US 1998-81709	19980519
CA 2333310	AA	19991125	CA 1999-2333310	19990519
AU 9938077	A1	19991206	AU 1999-38077	19990519
TR 200003438	T2	20010321	TR 2000-200003438	19990519
BR 9911046	A	20010424	BR 1999-11046	19990519
EP 1094818	A1	20010502	EP 1999-920510	19990519
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE, FI				
JP 2002515438	T2	20020528	JP 2000-549263	19990519
NZ 508991	A	20030926	NZ 1999-508991	19990519
NO 2000005835	A	20010118	NO 2000-5835	20001117
PRIORITY APPLN. INFO.:			US 1998-81709	A2 19980519
			WO 1999-CA449	W 19990519

OTHER SOURCE(S): MARPAT 132:458
AB When administered locally, tricyclic, second generation and third generation antidepressants, such as amitriptyline and desipramine, have been shown to produce analgesia in a subject having a site of local discomfort. The analgesic effect of such antidepressants, when administered locally is equal to that achieved by systemic administration and lasts longer. The invention provides compns. containing tricyclic, second generation and third generation antidepressants for local administration, such as those formulated for topical application, or for injection in slow-release delivery vehicles, and methods for their use for producing local analgesia. When administered locally onto a neuropathic paw, amitriptyline at a dose of 100 nmol showed antinociceptive effect, almost completely reversing the thermal hyperalgesia in nerve-injured rats without systemic effects. Despite considering the possibility of a potential involvement of antihistaminic, antiadrenergic, antiserotonergic, and anticholinergic actions in the action of amitriptyline, the only mechanism clearly implicated in the action of amitriptyline was some form of interaction with adenosine receptors as peripheral analgesia was partially blocked by the adenosine receptor agonist caffeine.

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **85650-52-8**, Mirtazapine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of tricyclic and second and third generation antidepressants for suppression of local analgesia)
RN 85650-52-8 CAPLUS
CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	61.64	217.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.40	-8.40

STN INTERNATIONAL LOGOFF AT 09:44:02 ON 21 SEP 2004